DETAILED ACTION

1. The Amendment filed December 10, 2008 in response to the Office Action of September 11, 2008 is acknowledged and has been entered. Claims 2-16 were previously withdrawn. Claims 1 and 17-24 are currently being examined.

Rejections Maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 17, 22, and 24 remain rejected under 35 U.S.C. 102(b) as being anticipated by Finlay et al. (J. of Cell Biol. July 1991, 114: 169-183) as evidenced by Cannon et al. (Urology June 2007, 69: 1227-30) and Appendix 1 for the reasons set forth in the Office Action of September 11, 2008, section 3, pages 2-4.

Examiner argued:

Finlay et al. teach a polyclonal antibody to the rat nuclear pore protein p54, which is detectably labeled with ^{125}I protein-A, see page 171-2nd col., 173-1st col. and Figure 2. The nuclear pore protein p54 of Finlay et al. is nucleoporin 54 (Nup54), see Appendix 1.

Cannon et al. teach that RCCA-1 is a differentially spliced form of Nup 54 identified by Ansorge et al., which is CAD97957 see Abstract, p. 1228-2nd col., reference 7, and Appendix 1. An alignment of CAD97957 with the rat Nup 54 shows that the two proteins have two regions of over 100 amino acids with nearly 100 % identity.

Although the reference does not specifically state that the antibodies are directed against RCCA-1, given that the polyclonal antibodies of Finlay et al. bind a polypeptide that has two regions of over 100 amino acids of nearly 100 % identity with RCCA-1, it would be expected that polyclonal antibodies that bind Nup 54 will bind RCCA-1, thus, the claimed antibodies appear to be the same as the prior art antibodies, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the method of the prior art does not possess the same material, structural and

functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed antibodies are different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

Applicants argue that to substantiate the rejections over Finlay (A) and Snow (B), the examiner invokes Cannon for disclosing that "RCCA-1 is a differentially spliced form of Nup 54 identified by Ansorge et al., which is CAD97957." Id. at page 5, lines 5 & 6. The examiner further alleges that "an alignment of CAD97957 with rat Nup 54 shows that the two proteins have two regions of over 100 amino acids of nearly 100% identity." Id. at page 5, lines 7 & 8. Based on his perception of shared identity, the examiner concludes that "it would [have been] expected that not only polyclonal antibodies but also a substantial portion of monoclonal antibodies that bind Nup 54 will bind RCCA- 1 ." Id., lines 11-13, and Appendix 1.

Applicants argue that concerning the rejection over Knapp (C), the examiner contends that Cannon had identified "RCCA-2 ... as GI: 763431, which is similar to human albumin," and that "[h]uman serum albumin is 99% identical to GI: 763431 over the first 455 amino acids." Id., lines 17-19. Given this understanding of the degree of sequence identity, the examiner asserts that "not only polyclonal antibodies but also a substantial portion of monoclonal antibodies that bind Nup 54 will bind GI: 763431/RCCA-2." Office Action at page 7, lines 1-2, and the examiner's "Appendix 2." Applicant respectfully traverses these rejections.

Applicants argue that the examiner's assertion that prior-art antibodies would bind the RCCA proteins is inapposite to applicant's claimed invention, because the antibodies of that invention do not recognize prior-art proteins, such as Nup 54. Compare Office Action at page 3, lines 18 - 20, page 5, lines 11 - 13 and page 7, lines 1 - 2. Whether the prior-art antibodies bind any of the RCCA proteins is of no moment, because these antibodies also detect their respective

targets in non-cancerous renal cells (see below). In sharp contrast, the claimed antibodies exclusively detect RCCA proteins in cancerous renal cells. In light of such dissimilarity in binding pattern, it necessarily follows that the claimed antibodies and the prior-art antibodies are different.

Applicant's arguments have been considered, but have not been found persuasive because Applicant is arguing limitations, exclusively detecting RCCA proteins in cancerous renal cells, that are not found in the claims. Furthermore, Applicant has not shown that there is any structural feature in the RCCA proteins in cancerous renal cells that would preclude the binding of the prior art antibodies.

Applicants argue that according to MPEP § 2131, a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior-art reference." Claim 1 is directed to antibodies that detect RCCA proteins that are "absent in normal renal cells but present in cancerous renal cells" (emphasis added). See also specification at page 22, lines 19-26, and Table 2. To the contrary, as noted above, all prior-art antibodies were generated using normal, non-pathological proteins as antigens, and all prior-art antibodies detect their respective target proteins in normal, non-pathological cells. See: Finlay, at page 17, right column, lines 37-45; Snow at page 1144, left column, lines 36-56, and fight column, lines 8-19; and Knapp at Figure 6a.

Applicants argue that as claimed, applicant's antibodies do not detect their respective targets in normal, non- pathological tissues. Failing to teach detection exclusively in cancerous renal cells, the cited art likewise fails to anticipate the claimed invention. For at least these reasons, applicant requests the rejection be withdrawn.

Applicant's arguments have been considered, but have not been found persuasive because Applicant is arguing limitations, not detect their respective targets in normal, non- pathological tissues, which are not found in the claims. Furthermore, Applicant has not shown that there is any structural feature in the RCCA proteins in cancerous renal cells that would preclude the binding of the prior art antibodies to the homologous sequences shared between the two protein.

3. Claims 1, 17, and 22-24 remain rejected under 35 U.S.C. 102(b) as being anticipated by Snow et al. (J. Cell Biol. 1 May 1987, 104: 1143-1156) as evidenced by Cannon et al. (Urology June 2007, 69: 1227-30) and Appendix 1 in the Office Action of September 11, 2008, section 4, pages 4-5.

Examiner argued:

Snow et al. teach monoclonal and polyclonal antibodies to the rat nuclear pore protein p54, , which is detectably labeled with ^{125}I protein-A, see Abstract, page 1144-1146., Figs. 1, 2, 4 and 5 and Table 1. The nuclear pore protein p54 of Snow et al. is nucleoporin 54 (Nup54), see Appendix 1.

Cannon et al. teach that RCCA-1 is a differentially spliced form of Nup 54 identified by Ansorge et al., which is CAD97957 see Abstract, p. 1228-2nd col., reference 7, and Appendix 1. An alignment of CAD97957 with the rat Nup54 shows that the two proteins have two regions of over 100 amino acids of nearly 100 % identity.

Although the reference does not specifically state that the antibodies are directed against RCCA-1, given that the polyclonal antibodies of Finlay et al. bind a polypeptide that has two regions of over 100 amino acids of nearly 100 % identity with RCCA-1, it would be expected that not only polyclonal antibodies but also a substantial portion of monoclonal antibodies that bind Nup 54 will bind RCCA-1, thus, the claimed antibodies appear to be the same as the prior art antibodies, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the method of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed antibodies are different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

Applicant applied the arguments set forth above to the instant rejection based on Snow et al. Thus, for the reasons set forth above, Applicant's arguments have not been found persuasive and the rejection is maintained.

4. Claims 1, 18, and 22-24 remain rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No.: 5,037,744 (Knapp et al. August 6, 1991) as evidenced by Cannon et al. (Urology June 2007, 69: 1227-30) and Appendix 2 in the Office Action of September 11, 2008, section 5, pages 5-7.

Examiner argued:

US Patent No.: 5,037,744 teaches polyclonal and monoclonal antibodies to human serum albumin and detectably labeling the antibodies see col. 3-lines 49-62, col. 1-lines 27-35, and cols. 14-15.

Cannon et al. (Urology June 2007, 69: 1227-30) teach RCCA-2 was identified as GI: 763431, which is similar to human albumin, see para. bridging p. 1228-1229. Human serum albumin is 99% identical to GI: 763431 over the first 455 amino acids, see appendix 2.

Although the reference does not specifically state that the antibodies are directed against RCCA-2, given that the polyclonal antibodies of US Patent No.: 5,037,744 bind a polypeptide that is 99% identical to GI: 763431/RCCA-2 over the first 455 amino acids, it would be expected that not only polyclonal antibodies but also a substantial portion of monoclonal antibodies that bind Nup 54 will bind GI: 763431/RCCA-2, thus, the claimed antibodies appear to be the same as the prior art antibodies, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the method of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed antibodies are different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

Applicant applied the arguments set forth above to the instant rejection based on Snow et al. Thus, for the reasons set forth above, Applicant's arguments have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1, 18, and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Menaya, J. et al. (Accession No AAA64922, GI: 763431, 10 April 1995), in view of Cannon et al. (Urology June 2007, 69: 1227-30), in view of Harlow and Lane (Antibodies, a Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988, p. 141-142, previously cited), and in further view of Sambrook et al. (Molecular Cloning: A Laboratory Manual, 1989, p. 18.70- 18.75, previously cited) in the Office Action of September 11, 2008, section 6, pages 7-10.

Examiner argued:

Menaya et al. teach Accession No AAA64922, GI: 763431.
Cannon et al. (Urology June 2007, 69: 1227-30) teach RCCA-2 was identified as GI: 763431, see para. bridging p. 1228-1229.
Harlow and Lane teach that the usefulness of monoclonal antibodies stems from three characteristics- their specificity of binding, their homogeneity, and their ability to be produced in unlimited quantities. The production of monoclonal antibodies allows the isolation of reagents with a unique, chosen specificity. Harlow and Lane teach that because all of the antibodies

produced by descendants of one hybridoma cell are identical, monoclonal antibodies are powerful reagents for testing for the presence of a desired epitope. Harlow and Lane teach that hybridoma cell lines also provide an unlimited supply of antibodies, see p.141.

Harlow and Lane teach that, although in theory monoclonal antibodies can be used for all of the tasks for which polyclonal antibodies are used, polyclonal antibodies are easier to produce and may be better for specific techniques, see p. 142, first para., and Table 6.1.

Sambrook et al. teach detectably labeling antibodies for immunological detection of proteins by western blots, see p. 18.70-18.75.

It would have been *prima facie* obvious to one of ordinary skill in the art to have produced antibodies to GI: 763431because the Board of Patent Appeals and interferences has taken the position that once an antigen has been isolated, the manufacture of antibodies against it is *prima facie* obvious. See Ex parte Ehrlich, 3 USPQ 2d 1011 (PTO Bd. Pat. APP. & Int. 1987), Ex parte Sugimoto, 14 USPQ 2d 1312 (PTO Bd. Pat. App. & Int. 1990).

Additionally, it would have been *prima facie* obvious and one of ordinary skill in the art would have been motivated to make monoclonal antibodies to GI: 763431 because Harlow and Lane teach the advantages of having an unlimited supply of homogeneous antibodies that have a defined specificity. Additionally, one would have been motivated to produce polyclonal antibodies to GI: 763431 because Harlow and Lane teach that polyclonal antibodies are easier to produce than monoclonal antibodies and may be more useful for specific immunological techniques. Given the conventional nature of the production of monoclonal and polyclonal antibodies at the time the invention was made, one would have had a reasonable expectation of successfully producing monoclonal and polyclonal antibodies against GI: 763431.

Further, it would have been prima facie obvious and one would have been motivated to label the antibodies for use in the well known art method of western to detect GI: 763431. using antibodies that are directly or indirectly labeled with a secondary antibody or other reagent, see Sambrook et al. p. 1870-1875.

Thus, one of skill in the art would be motivated with a reasonable expectation of success to make labeled monoclonal or polyclonal antibodies to the proteins GI: 763431.

Applicants argue that the examiner's presumption that RCCA-2/GI: 763431 are identical is faulty, as applicant has demonstrated above. The albumin sequence of Maneaya (GI: 763431) was obtained from "normal" human liver tissue, as Appendix 2 indicates, while Cannon explicitly describes RCCA-2 as an "altered form of albumin" found in cancerous renal tissue (page 1229 at ¶ 4; emphasis added). When Cannon is read in its entirety, therefore, it is apparent that RCCA-2 must differ from the albumin protein of "normal" cells, GI:763431.

Applicants argue that cannon does not identify any specific "alteration" to RCCA-2 that limits expression (and, hence, detection in accordance with this invention) to cancerous renal

cells. Nor does the reference disclose the RCCA-2 sequence, per se. Accordingly, the prior-art fails sufficiently to describe the "altered albumin," RCCA-2, in a manner that renders the claimed antibodies obvious, within the meaning of Section 103. For at least these reasons, Applicant request the rejection be withdrawn.

Applicant's arguments have been considered, but have not been found persuasive. Cannon et al. teach that the most likely identification of RCCA-2 was gi:763431, which is similar to human albumin, i.e. gi:763431 is not normal human albumin, but is RCCA-2, see p. 1229-left col. Given that gi:763431was known in the art and given that neither the specification nor the art of record shows that gi:763431 is distinct from RCCA-2 in cancer cells, it would have be obvious to make antibodies to gi:763431 that would also recognize RCCA-2 for the reasons previously set forth. Applicant's arguments have not been found persuasive and the rejection is maintained.

6 All other objections and rejections recited in Office Action of September 11, 2008 are withdrawn.

7. Claims 19-21 are objected to as being dependent upon a rejected base claim, but would appear to be allowable if rewritten in independent form including all of the limitations of the base claim.

8. No claims allowed.

9. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal form, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Peter J. Reddig
Examiner
Art Unit 1642

/Karen A Canella/

Primary Examiner, Art Unit 1643

PJR